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Castleman's Disease of the Mesentery in a Child: A Case of Seven Years' Duration Without Typical X-Ray Findings

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This report describes a 9-year-old boy with intermediate variant type of giant lymph node hyperplasia or Castleman's disease (CD) originating from the mesentery. He had symptoms and signs related to the disease for seven years before the final diagnosis.

The patient's general condition remained good, except for periods of fever and abdominal pain. Pallor and slow growth were the only abnormal findings on physical examination during the follow-up. Laboratory measurements showed worsening microcytic anemia, low serum iron level, and low iron stores in bone marrow samples. The erythrocyte sedimentation rate (ESR) increased to 110 mm/h, and the serum levels of C-reactive protein varied between 80 and 120 mg/l. The level of serum albumin was low, 25–28 g/l, and serum immunoglobulin G was somewhat elevated, varying between 17–13 g/l.

The radiologic examination of intestine gave pathological results suggesting a small bowel disease, but no tumor was detected.

The abnormal laboratory values and symptoms of the patient resolved completely after surgical removal of the mass. Med. Pediatr. Oncol. 28:362–365, 1997.

Key words: Castleman's disease; hematological manifestations

INTRODUCTION

Castleman et al. [1,2] described the disease known as giant lymph node hyperplasia, also known as lymphoid hamartoma. Although it has been reported at all ages, most patients are between 30 and 40 years of age at presentation [3]. There are two recent reviews on Castleman's disease (CD) in children. Salisbury [4] found 12 cases concerning children less than 14 years of age, and O'Reilly and colleagues [5] identified additional 17 cases in children in the same age group.

CD can be divided into three types on the basis of clinical features and histological findings: hyaline vascular type, plasma cell type, and intermediate variant type [6,7]. The plasma cell type seems to be more common in children than in adults, accounting for approximately 50% of cases in children as compared with only 10% in adults [5]. The plasma cell type has been associated with a wide spectrum of systemic symptoms and signs such as malaise, growth retardation, anemia, thrombocytosis, elevated erythrocyte sedimentation rate (ESR), and hypergammaglobulinemia [8,9]. All of these findings are also typical for inflammatory bowel disease (IBD) in children [10]. The systemic manifestations of CD have been attributed to the elevated serum levels of interleukin-6, tumor necrosis factor-beta, gamma-interferon mRNA [11].

CD usually appears as a localized form, especially in children. In contrast to the relatively benign clinical course of the localized forms, the multicentric form of the disease carries significant morbidity and mortality [4,5].

The most common sites for CD in childhood and adolescence are the abdomen, the mediastinum, and the hila of the lungs. As with adult cases, most pediatric cases are detected incidentally or because of local growth producing a mass [4]. Early diagnosis of mesenteric CD is difficult, especially in children [12]. This is reflected in the long-standing nature of many of the cases, Goebel et al. [13] and Bjarnason et al. [8] reporting cases of 20 years' and 11 years' duration, respectively.

This report describes a 9-year-old boy with intermediate variant type of CD originating from the mesentery. He had symptoms and signs related to the disease for seven years before the final diagnosis. Pathological findings were made on intestinal x-rays, suggesting on IBD,

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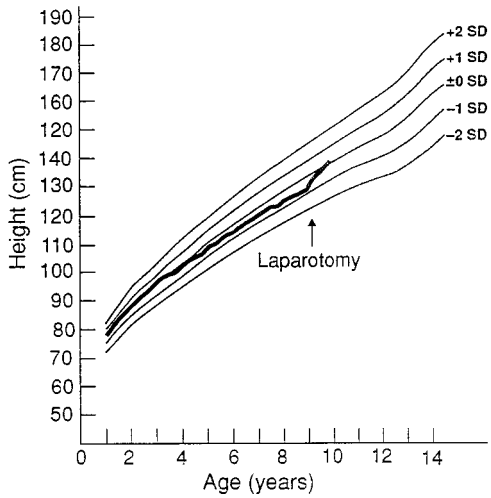

Fig. 1. The patient's standing height during follow-up, expressed in centimeters and as the standard deviation (SD) score from the mean for age and sex (Finnish height score).

and no tumor was detected. The abnormal laboratory values and symptoms of the patient resolved completely after surgical removal of the mass.

CASE HISTORY

Clinical and Laboratory Features

A 2-year-old boy was admitted to the hospital in November 1987, for evaluating the cause of his anemia (hemoglobin 9.2 g/dl, hematocrit 28%) and elevated ESR (80 mm/h). Previously, in Feburary 1986 when he had fever, his hematocrit had been 36%, which was normal for his age of six months. From August to October 1987 he has had periodic feverish diarrhea.

At the examination and subsequent check-ups, the patient's general condition was quite good except for periods of fever and abdominal pain. Pallor and growth failure (Fig. 1) were the only abnormal findings on physical examinations during follow-up.

Serial investigations were performed during the period 1987–1993. The laboratory findings are summarized in Table I. The laboratory tests showed worsening microcytic anemia, low serum iron level, and low iron stores in the bone marrow samples. Serum ferritin levels were normal. The iron absorption curve after oral administration of ferrous sulfate (dose 1 mg/kg) was flat. These findings suggested anemia associated with a chronic disease.

The platelet count tended to rise during the follow-up. ESR increased to 110 mm/h, and the serum levels of C-reactive protein varied between 80 and 120 mg/l. The level of serum albumin was low, 25–28 g/l, and serum immunoglobulin G (IgG) was somewhat elevated, 17–13 g/l, through the years before the laparotomy.

Chest radiographs showed no mediastinal mass. Abdominal ultrasound, repeated five times, last in June 1994, revealed no pathological mass. There was, however, evidence of splenomegaly in the last two ultrasound investigations. Abdominal computed tomography (CT) in April 1992 was normal.

A barium meal follow-through was undertaken three times (12/1987, 11/1990, and 3/1994). The first examination revealed benign lymphoid hyperplasia throughout the small intestine. In the following two examinations there were non-uniform nodular filling defects, each measuring four or more mm in diameter, exceeding in number (Fig. 2). Those were indicated of IBD.

Colonoscopy, repeated four times, revealed no abnormality in the intestine. Histopathological examination of intestinal biopsies were also normal. However, no biopsy could be obtained from the part of the ileum with a pathological finding on contrast medium examination. Esophagogastroscopy, undertaken four times, was normal.

The hydrogen breath test showed a substantial rise in the concentration of hydrogen 240 minutes after the test meal. However, as the patient experienced no abdominal symptoms during the test, the result suggested malabsorption but no intolerance of lactose.

Because of suspected latent infection, adenoidectomy was performed two times. Additionally, tonsillectomy was done but it produced no improvement of laboratory values.

During the first months of 1994, the patient became more tired, growth delay became more evident, and more delayed, and he had abdominal pain daily. On the basis of the x-ray findings, suggesting Crohn's disease and with worsening symptoms or other IBD, he received prednisone 1.2 mg/kg/d in three divided doses for six weeks. The ESR decreased temporarily to 50 mm/h, but increased soon to the level of 90–100 mm/h. Crp remained at the previous level of 80–100 mg/l, and Hb and serum albumin were low. Azathioprine 2 mg/kg/d in two divided doses was then administered for five weeks without any effect. The therapy with prednisone was at the same time tapered and discontinued over six weeks.

Surgery

Because of the lack of exact diagnosis and continuing periodic abdominal pain, explorative surgery was performed. The laparotomy revealed a spherical mass 5 cm in diameter in the mesentery of the ileum near the ligament of Treitz. A few adjacent lymph nodes appeared slightly enlarged. Splenomegaly was also evident. The patient received one unit of red cells after the operation.

The patient made an uneventful recovery after surgery and has been well since. Two months postoperatively, the laboratory values had normalized and remained nor-

TABLE I. Laboratory Findings Before and After The Removal of the Mesenteric Mass

	Date									
	II/86	XI/87	III/89	XI/92	I/94	V/94	Laparotomy 13.IX/94 30.IX/94	XI/94	I/95	VI/95
Hb (g/dl)	N.D.	92	100	87	79	85	109	114	126	124
Hematocrit (%)	36	28	30	N.D.	28	31	38	35	41	41
MCV (fl)	N.D.	63	63	N.D.	60	62	67	70	73	79
Platelets ($\times 10^9$/l)	173	493	454	524	565	730	345	296	261	258
WBC ($\times 10^9$/l)	9.3	9.8	N.D.	N.D.	7.7	16.4	6.7	5.6	6.7	5.6
C-reactive prot (mg/l)	0	11	27	100	120	85	6	6	N.D.	6
ESR (mm/h)	N.D.	50	72	102	110	52	6	9	9	5
Albumin (g/l)	N.D.	28	28	N.D.	26	30	N.D.	36	38	39
IgG (g/l)	N.D.	15	15	17	13	N.D.	N.D.	8	8	N.D.
Ferritin (μg/l)	N.D.	N.D.	40	N.D.	48	N.D.	N.D.	6	6	N.D.
Serum iron (μmol/l)	N.D.	2	2.5	N.D.	2.3	N.D.	11.0	6	5.3	7.4

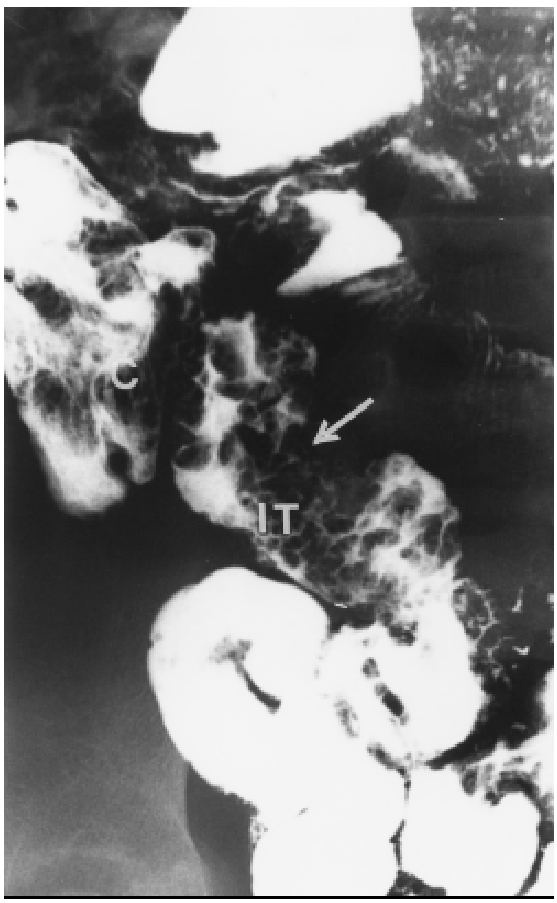

Fig. 2. Multiple non-uniform nodular filling defects (White arrow) in the barium column of the terminal ileum (IT); C = Cecum.

mal during a follow-up period of twelve months. The patient has had a growth spurt (Fig. 1), and his abdominal symptoms have disappeared. Nevertheless, seven months after the operation he developed intestinal obstruction due to adhesions. Laparotomy carried out to liberate the bowel, yielded no other abnormal findings.

Pathological Findings

Pathological examination showed giant lymph node hyperplasia of mixed plasma cell and hyaline vascular histology or Castleman's disease, intermediate type.

DISCUSSION

The clinicopathological findings of our patient are consistent with previously reported cases, among which the intermediate variant is less frequent.

We suspected CD on the basis of the patient's microcytic anemia, hypersedimentation, high level of IgG and retarded growth, but the normal findings on abdominal ultrasound and CT (excluding splenomegaly) brought uncertainty into the diagnostic procedure. Also, the clinical and laboratory findings made are typical of IBD, which was therefore intensively looked for.

The diagnosis of Crohn's disease localized in the terminal ileum is complicated. In our case, the failure of the endoscopic examination of the terminal ileum further confounding the differential diagnosis. However, no granulomas were seen in any biopsy specimens from other parts of the gastrointestinal tract.

The fact that we based our preliminary diagnosis of Crohn's disease solely on radiology can be criticized in this case. Exploratory laparotomy should perhaps have been done before starting the treatment trial for IBD.

We agree with Ferreiros and colleagues [14] that CT is a valuable technique in detecting abdominal lymphadenopathy. The enhancing characteristics of the mass may be helpful in establishing the diagnosis. Unfortunately the result of abdominal CT was not satisfactory because of the movement blur from noncooperation inherent pediatric practice.

Several authors have recommended abdominal CT or even exploratory laparotomy in children with growth retardation, hypergammaglobulinemia, and anemia

[5,12,14,15,16,17]. While supporting this advice we would like to emphasize the role of exploratory laparotomy in cases with a typical history. The role of magnetic resonance (MR) imaging in the evaluation of pediatric abdominal masses should still be regarded as experimental. MR imaging suffers from two disadvantages. First, it is expensive, and second, because of motion, one cannot obtain exquisite images in all patients. So, the role of MR is not completely defined.

The features of pseudopolyposis on x-ray of the ileum, suggesting Crohn's disease, have not been described before in connection with GLNH. The disappearance of the abdominal symptoms after surgery indicates that they may be or may refer secondary importance.

A slight decrease in ESR, but no improvement in clinical symptoms, was noticed during prednisone therapy. This finding bears a similarity with the case report of Massey et al. [18]. These authors described a girl with a temporary increase in hemoglobin values during steroid therapy. The immunological and inflammatory dimensions of CD may explain these incidental findings.

An interesting feature in our case, the ultrasound examination suggested splenomegaly, which in turn would point to the possibility of lymphoma. Hung et al. [11] have described hepatosplenomegaly associated with a case of plasma cell type CD. The exact cause of these findings in unknown.

Development of lymphoma has been reported especially in patients with multicentric CD [19], but also in a case of localized disease [20]. This finding stresses the importance of long-term follow-up of these patients.

In conclusion, recognition of localized CD is important because the associated anemia and all systemic manifestations can be treated successfully by surgical removal of the mass.

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